Practice Tool #2 – Definitions of CEV/ Immunosuppressed

CLINICALLY EXTREMELY VULNERABLE	
General Information	
Clinically Extremely Vulnerable (CEV) criteria were developed by a group of provincial experts caring for patients with conditions such as cancer, cystic fibrosis, organ transplant and renal disease, for the purpose of identifying those who should be prioritized for vaccination. Patients in the CEV category have been receiving information related to their vaccine eligibility which has identified them as CEV. Patients usually will know if they are CEV and can identify what condition or medication they have which makes them CEV. There are three CEV Groups: 1, 2 and 3. Group 1 are patients 12 and older who are severely immunosuppressed due to conditions such as haematological malignancies on active treatment or solid organ transplantation. Group 2 are patients 12 and older with moderate immunosuppression. Group 3 contains individuals with heterogeneous conditions who are not immunosuppressed, but who are at high risk of complications from COVID-19. CEV categories were developed in 2020 and patients are not removed from these lists as they continue to require subsequent vaccinations. However, ***patients who are categorized as CEV may not be eligible for treatment if they are no longer immunosuppressed or at risk.*** *Please consult the precise CEV definition that would make a patient eligible for treatment, paying particular attention to the time periods and notes.*	
CEV 1	
Definition	**Notes**
Solid Organ Transplant (SOT) recipients: Solid organ transplant recipients of kidney, liver, lung, heart, pancreas or islet cell, bowel or combination transplant.	
Those being actively treated for hematological malignancy: Have received or are receiving active treatment (chemotherapy, targeted therapies including CAR-T, immunotherapy) for malignant hematologic conditions (e.g., leukemia, lymphoma, or myeloma).	Have received treatment for haematological malignancy in the ***last year*** These medications may not come up on PharmaNet as they are administered in hospital facilities such as BC Cancer
Those who have had a bone marrow or stem cell transplant: Have had bone marrow or stem cell transplant or are still taking immunosuppressant medications related to transplant.	Have received a BMT/HSCT ***in the last two years*** or who are currently on immunosuppressants for graft vs. host disease (GVHD)

	Patients with HSCT more than two years ago are included in the CEV category 3
Those who have taken anti-CD20 agents or B-cell depleting agents which cause suppression of their immune response: i. Have received treatment with any anti-CD20 agents (i.e., rituximab, ocrelizumab, ofatumumab, obinutuzumab, ibritumomab, tositumomab) or ii. B-cell depleting agents (i.e., epratuzumab, MEDI-551, belimumab, BR3-Fc, AMG-623, Atacicept, anti-BR3, alemtuzamab).	Have received anti-CD20 or B-cell depleting agents ***in the last two years*** These medications may not come up on PharmaNet as they are administered in hospital facilities such as BC Cancer and/or could have been given over 14 months ago
Those with severe primary immuno-deficiencies: Have combined immune deficiencies affecting T-cells, immune dysregulation (particularly familial hemophagocytic lymphohistiocytosis) or those with type 1 interferon defects (caused by a genetic primary immunodeficiency disorder or secondary to anti-interferon autoantibodies).	There are less than 100 individuals in this category in BC
CEV 2	
Definition	**Notes**
Those additional patients who have received treatment for cancer including solid tumors: i. Have received or are receiving systemic therapy (including chemotherapy, molecular therapy, immunotherapy, targeted therapies including CAR-T, monoclonal antibodies other than the hematological malignancies in CEV 1, *EXCEPT* those receiving adjunctive hormonal therapy ONLY ii. Have received or are receiving radiation therapy for cancer.	Systemic cancer therapy *received in the last 6 months* Radiation *received in the last 3 months*
Those who have taken significantly immunosuppressing drugs: i. Anti-CD20 agents: rituximab, ocrelizumab, ofatumumab, obinutuzumab, ibritumomab, tositumomab; ii. B-cell depleting agents: epratuzumab, MEDI-551, belimumab, BR3-Fc, AMG-623, Atacicept, anti-BR3, alemtuzamab;	Anti-CD20 agents *taken in the last 2 years* B-cell depleting agents *taken in the last 2 years* Anti-CD20 and B-cell depleting agents may not be on PharmaNet

iii. Biologics: abatacept, adalimumab, anakinra, benralizumab, brodalumab, canakinumab, certolizumab, dupilumab, etanercept, golimumab, guselkumab, infliximab, interferon products (alpha, beta, and pegylated forms), ixekizumab, mepolizumab, natalizumab, omalizumab, resilizumab, risankizumab, sarilumab, secukinumab, tildrakizumab, tocilizumab, ustekinumab, or vedolizumab; iv. Oral immune-suppressing drugs: azathioprine, baricitinib, cyclophosphamide, cyclosporine, leflunomide, dimethyl fumerate, everolimus, fingolimod, mycophenolate, siponimod, sirolimus, tacrolimus, tofacitinib, upadacitinib, methotrexate, or teriflunomide; v. Oral steroids on an ongoing basis: dexamethasone, hydrocortisone, methylprednisolone, or prednisone; vi. Immune-suppressing infusions/injections: cladribine, cyclophosphamide, glatiramer, methotrexate	Biologics *taken in the last 3 months* Oral immunosuppressing drugs taken *in the last month* Oral steroids *equivalent to 20mg/d of prednisone equivalent (adult dose) taken on an ongoing basis in the last month* Infusions/injections in point number vi. taken *in the last 3 months*
Those with advanced untreated HIV infection or those with acquired immuno-deficiency syndrome (AIDS) defined as AIDS defining illness or CD4 count ≤ 200/mm^3 or CD4 fraction ≤ 15%	Untreated HIV or treated HIV with CD4 count ≤ 200/mm^3 qualifies the patient for treatment but referral to an HIV Specialist is recommended due to complexity of patients and drug-drug interactions. However, treatment with nirmatrelvir/ritonavir should not be withheld or delayed.
People with moderate primary immunodeficiencies: Have a moderate to severe primary immunodeficiency which has been diagnosed by an adult or pediatric immunologist and requires ongoing immunoglobulin replacement therapy (IVIg or SCIG) or the primary immunodeficiency has a confirmed genetic cause (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome).	IVIg and SCIg treatment will not be visible on PharmaNet There are <1000 such patients in BC
Those with on dialysis and those with severe kidney/renal disease: i. Dialysis (hemodialysis or peritoneal dialysis); ii. Stage 5 chronic kidney disease (eGFR <15ml/min);	Patients with renal disease are not eligible to receive nirmatrelvir/ritonavir as it is contraindicated in severe renal disease. Remdesivir should be used in patients who are CEV 2 who cannot take nirmatrelvir/ritonavir, including those with renal disease if their risk of

iii. Glomerulonephritis and receiving steroid treatment	hospitalization from COVID-19 is ≥ 5%. Refer to the Clinical Practice Guide to estimate risk based on age, vaccine status and CEV status. CEV 2 patients who meet this level of risk include individuals who: • Are ≥ 50 years old regardless of vaccine status • Have received 0-2 doses of a COVID-19 vaccine
CEV 3	
Definition	**Notes**
Patients with severe respiratory disorders: i. Cystic fibrosis, ii. Severe COPD: hospitalized because of COPD iii. Severe asthma: hospitalized because of asthma iv. Are taking biologics for asthma, severe lung disease and at least one of the following: long-term home oxygen; assessment for a lung transplant; severe pulmonary arterial hypertension; severe pulmonary fibrosis/interstitial lung disease.	Hospitalized for COPD *in the last year* Hospitalized for asthma *in the last year* Taking biologics *in the last 3 months*
Rare blood disorders: Homozygous sickle cell disease, highest risk thalassemia (Received an attestation letter. *The full definition is:* a diagnosis of thalassemia and two of the following: transfusion dependent; receiving iron chelation therapy; pre-transfusion hemoglobin levels <70 in last 2-3 years; have iron overload; have had a splenectomy or have other significant health conditions; are over 50, Atypical Hemolytic Uremic Syndrome or Paroxysmal Nocturnal Hemoglobinuria)	There are <200 people in BC with these disorders. The full definition is for completeness. Patients will have received communication from Bonnie Henry if their rare blood disorder qualifies.
Rare metabolic disorders: certain metabolically unstable inborn errors of metabolism: urea cycle defects; methylmalonic aciduria; propionic aciduria; glutaric aciduria; maple syrup urine disease.	There are only 87 patients in this category
Had a splenectomy: Anatomical or functional asplenia	
Diabetes treated with insulin	This is the largest CEV category and comprises of both Type 1 and Type 2 diabetes
Hematological and other cancers not captured in CEV group 1 or 2	This is a very broad category. ***It is important to distinguish whether the patient with cancer fits into***

	category 1, 2 or 3 *as age and vaccine status is not a consideration for remdesivir treatment in category 1, whereas only patients who are over 50 or have received 0-2 vaccine doses would qualify for remdesivir if nirmatrelvir/ritonavir are contraindicated if they are CEV 2 or 3.* *Examples of cancers here are chronic hematological malignancies under surveillance (e.g., chronic lymphocytic leukemia) or active solid tumours or metastatic cancer not on treatment but undergoing surveillance.*
Significant developmental disabilities: Down Syndrome, or Cerebral Palsy, or Intellectual Developmental Disability (IDD), or receiving supports from: • Community Supports for Independent Living (CSIL) or • Community Living British Columbia (CLBC): currently receiving supports or assessed and eligible for CLBC supports or • Nursing Support Services program for youth aged 16 and above • People aged 12+ whose condition is described but are not using support services can receive priority through consultation with their health-care provider (attestation form)	
Pregnant and have a serious heart disease, congenital or acquired, that requires observation by a cardiac specialist throughout pregnancy	Reproductive Infectious Diseases specialist on call at BCWH can be consulted for assistance with this group as needed as no therapy is specifically approved in pregnancy.
Neurological or other conditions causing significant muscle weakness around lungs requiring the use of a ventilator of continuous Bi-level positive airway pressure (Bi-PAP)	